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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,358	12/03/2003	Richard N. Kolesnick	1216-1-006CIP	5499

23565 7590 05/16/2006

KLAUBER & JACKSON
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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/727,358	KOLESNICK ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *8 and 21-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply w/seq*.

DETAILED ACTION

Non-Final Rejection

Claims 1-33 are pending.

The amendment to the specification filed on 4/3/06 is acknowledged and considered by the examiner.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-20, SEQ ID NO: 5) in the reply filed on 4/3/06 is acknowledged. The traversal is on the ground(s) that the examiner failed to define composition and/or methods with properties so distinct as to warrant separate examination and search. Each of antisense oligonucleotides target and modulate the expression of KSR. Applicant asserts that at least SEQ ID NO: 28 and SEQ ID NO: 8 be rejoined with the elected sequences because these sequences are exemplary of SEQ ID NO: 5. In addition, it would not be an undue burden to search the method and compositions because the additional search of the method would result in a search of identical classes wherein the oligonucleotides are classified. This is not found persuasive because other than the assertion by applicant that the examiner failed to define products and methods with properties so distinct as warrant separate examination the applicant does not point out why the groups are not distinct. With respect to applicant's argument that SEQ ID NO: 28 be rejoined with the elected, the argument is not found persuasive because SEQ ID NO: 28 is not recited in the instant claims. In response to applicant's argument that SEQ ID NO: 8 be rejoined with SEQ ID NO: 5, the argument is not found persuasive because SEQ ID NO: 8 is directed to a distinct oligonucleotide and a search for SEQ ID NO: 5

would not overlap with a search for SEQ ID NO: 8. In response to applicant's argument that it would not be an undue burden to search all of the oligonucleotide because the oligonucleotides target and modulate the expression of KSR. The argument is not found persuasive because this argument has already been addressed in the previous office action. Thus, the argument is not found persuasive for the reason(s) of record (see page 7 of the election/restriction). In response to applicant's argument that there is no undue burden to search product and methods together because searching the method would involve also searching the products. The argument is not found persuasive because searching the product does not require searching the method of using the product. The method may be novel and unobvious in view of the preamble or active step(s). In addition, it would be an undue burden to search both the product and method because each invention is classifiable in a different class and subclass.

The requirement is still deemed proper and is therefore made FINAL.

SEQ ID NO: 1 and 25 in claim 6, the term "121 to 141 of the sequence of human KSR" and SEQ ID NOs: 3, 27, and 4 in claim 7, claim 8, and claims 21-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/3/06.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or

more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention, which is also disclosed, in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/384,228, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

SEQ ID NO: 5 in instant claim 7 does not have written supporting provisional '228.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claim 17 is objected to because of the following informalities: the phrase "an antisense oligonucleotide of claim 1" is an improper phrase for a dependent claims. Suggest replacing the phrase with – the antisense oligonucleotide of claim 1 --. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "corresponding to 214 to 231 of the sequence of mouse KSR (SEQ ID NO: 5)" in claim 7 is a relative term, which renders the claim indefinite. The term "corresponding to 214 to 231 of the sequence of mouse KSR (SEQ ID NO: 5) " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The metes and bounds of the claims are undefined because it is not apparent to the skilled artisan whether the term is limited to SEQ ID NO: 5 or whether SEQ ID NO: 5 is an example of a sequence corresponding to 214 to 231 of the mouse KSR.

The term "187 to 204 of the sequence of human KSR" in claim 8 is a relative term which renders the claim indefinite. The term "187 to 204 of the sequence of human KSR" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite

degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Nucleotides 187 to 204 of human KSR is relative to a human KSR gene. The art of record teaches that there are several human SKR genes with different base pair lengths or polymorphisms. Thus, it is not apparent what nucleotides of a human KSR gene are being defined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The limitation "capable of expressing a nucleic acid which is substantially complementary to the coding sequence of KSR RNA, or portion/fragment thereof, wherein said oligonucleotide/nucleic acid inhibits the expression of KSR" in claims 15 and 20 and the phrase "capable of expressing a nucleic acid which is substantially complementary to the CA1 region of the coding sequence of KSR RNA, or portion/fragment thereof, wherein said oligonucleotide/nucleic acid inhibits the expression of KSR" in claim 16 does not have patentable weight over the prior art because the limitation(s) is directed to an intended use of the vector. See MPEP 2111-2111.02.

The term "pharmaceutical" and "therapeutically effective amount" in claim 17 does not have patentable weight over the prior art. See MPEP 2111-2111.02.

The oligonucleotide in claims 1-5, 7, and 9-20 reads on any nucleic acid sequence that hybridizes to KSR RNA (e.g., human SKR RNA) because of the term "comprising" and "substantially complementary".

In addition, in view of the term "portion thereof" in claims 6, 7, 12, 13, and 14, the oligonucleotide in the claims read on any nucleic acid that hybridizes to KSR RNA.

Claims 1-4, 11, and 15-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Monia et al. (US 20030109466). Monia teaches an antisense molecule which is complementary to a region of human KSR RNA (pages 1 and 42). Monia teaches the limitation in instant claim 4 (page 2). Monia teaches the limitation in claim 11 (page 4). Monia teaches the limitation in instant claim 19 (page 15). Monia teaches a vector in claims 15, 16, and 20 (page 1). Monia teaches the limitation in claims 17, 18 and 20 (page 8).

Claim 1-7 and 15-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Rubin et al. (US 5,747,288). Rubin teaches a polynucleotide sequence that comprises a nucleotide sequence is 100% identical to SEQ ID NO: 5. The polynucleotide sequence encodes Kas protein (which would include the CA1 region, translation initiation site, coding region, etc.). Rubin teaches a nucleic acid sequence that hybridizes to SEQ ID NO: 5 (column 63). The nucleic acid sequence comprises the same structure as the oligonucleotide recited in the instant claims. In addition, Rubin teaches a vector (columns 63-64).

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

MPEP 2112.01:

PRODUCT AND APPARATUS CLAIMS X WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TOTHAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS AREPRESUMED TO BE INHERENT

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monia et al. (US 20030109466) taken with Schuurs et al. (US 4,016,043). Monia teaches an antisense molecule which is complementary to a region of human KSR RNA (pages 1 and 42). However, Monia does not specifically teach labeling the molecule with an enzyme.

However, at the time the invention was made, Schuurs teaches a method for labeling a molecule for use in a detection method comprising attaching an enzyme to the molecule (columns 1-4).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Monia taken with Schuurs, namely to produce the oligonucleotide with a detection label (e.g., enzyme). One of ordinary skill in the art would have been motivated to combine the teaching for detecting the oligonucleotide in a cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 12-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monia et al. (US 20030109466) taken with Srivastava (US 6,261,834). Monia teaches an antisense molecule which is complementary to a region of human KSR RNA (pages 1 and 42). However, Monia does not specifically teach a recombinant DNA molecule comprising a nucleic acid sequence that encodes on transcription an antisense RNA complementary to mammalian KSR or portion thereof.

However, at the time the invention was made, Srivastava teaches an AAV vector comprising a gene encoding antisense RNA (column 21). The most significant advantages of AAV-based vectors are that they mediate integration into the host chromosomal DNA in a site-specific and stable manner (column 2).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Monia taken with Srivastava, namely to produce the recombinant DNA molecule. One of ordinary skill in the art would have been motivated to combine the teaching for stable and long-term expression of the recombinant DNA molecule.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, SPE – Art Unit 1635, can be reached at (571) 272-4517.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Brian Whiteman

BRIAN WHITEMAN
PATENT EXAMINER

Notice to Comply	Application No. 10/727358	Applicant(s) KOLESNICK et al.	
	Examiner B. Whiteman	Art Unit 1635	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set in the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See Raw sequence listing error report.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the specification**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-2510
For CRF Submission Help, call (571) 272-2501/2583.
PatentIn Software Program Support
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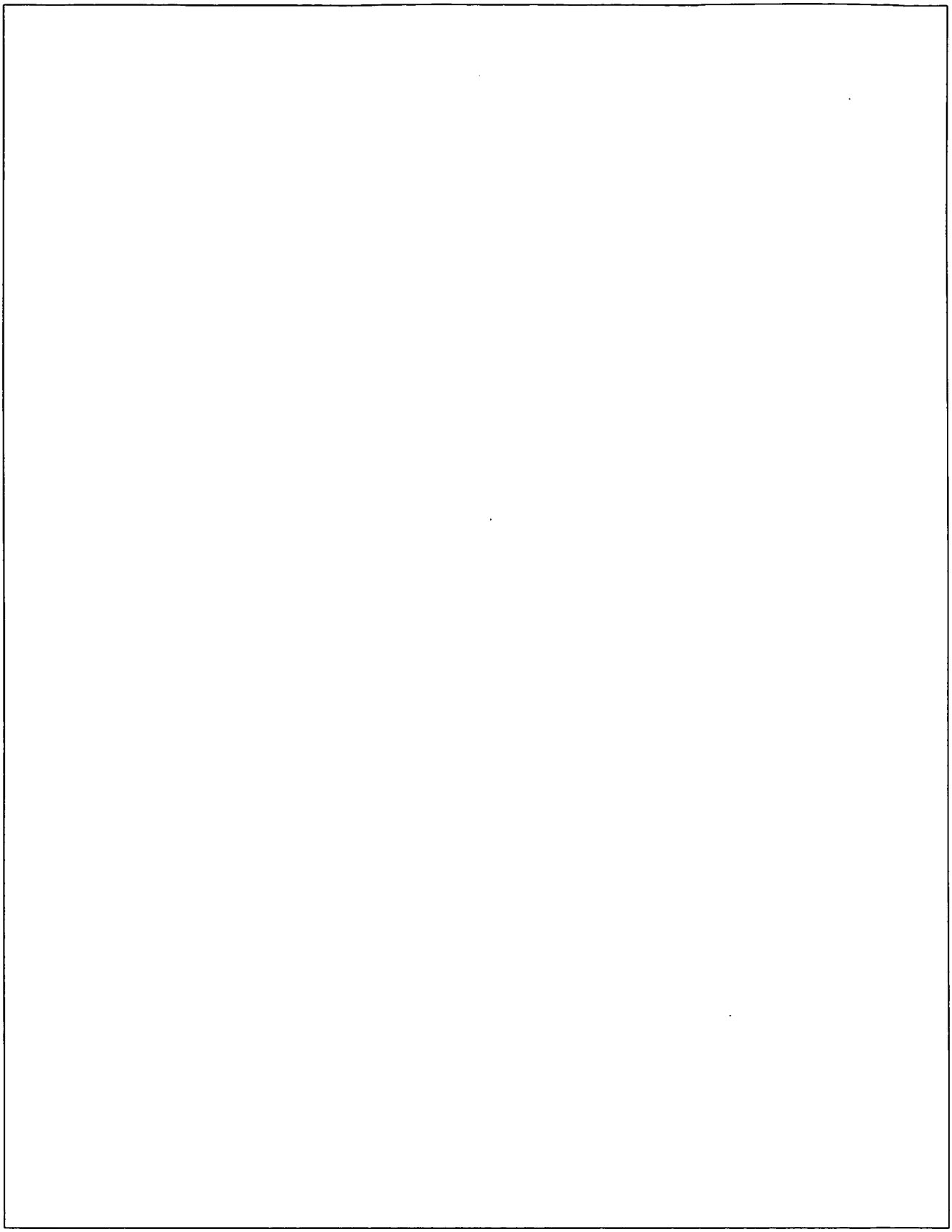
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY



STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/727,358A
Source: IFW16
Date Processed by STIC: 4-5-06

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO **REDUCE** ERRORED SEQUENCE LISTINGS, **PLEASE** USE THE **CHECKER VERSION 4.4.0 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
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Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>**, **EFS Submission User Manual** - ePAVE)
2. **U.S. Postal Service:** Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. **Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):** U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/10/06

IFW16

RAW SEQUENCE LISTING DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:31

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Does Not Comply
Corrected Diskette Needed
(pg. 6)

<110> APPLICANT: Kolesnick, Richard N.
Xing, Hong-Mei R.
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for Therapy of Ras Mediated Tumorigenesis
<130> FILE REFERENCE: 1216-1-006CIP
<140> CURRENT APPLICATION NUMBER: 10/727,358A
<141> CURRENT FILING DATE: 2003-12-03
<150> PRIOR APPLICATION NUMBER: 60/384,228
<151> PRIOR FILING DATE: 2002-05-30
<150> PRIOR APPLICATION NUMBER: 60/460,023
<151> PRIOR FILING DATE: 2003-04-03
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<151> PRIOR FILING DATE: 2003-05-29
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RAW SEQUENCE LISTING DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:31

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93 <220> FEATURE:
94 <223> OTHER INFORMATION: antisense oligonucleotide
96 <400> SEQUENCE: 7
97 gaggtcgtta gacactga 18
99 <210> SEQ ID NO: 8
100 <211> LENGTH: 16
101 <212> TYPE: DNA
102 <213> ORGANISM: Artificial Sequence
104 <220> FEATURE:
105 <223> OTHER INFORMATION: antisense oligonucleotide
107 <400> SEQUENCE: 8
108 ctttgcctct agggtc 16
110 <210> SEQ ID NO: 9
111 <211> LENGTH: 873
112 <212> TYPE: PRT
113 <213> ORGANISM: Mus musculus
115 <400> SEQUENCE: 9

```
116 Met Asp Arg Ala Ala Leu Arg Ala Ala Ala Met Gly Glu Lys Lys Glu
117  1               5                  10                  15
118 Gly Gly Gly Gly Gly Ala Ala Ala Asp Gly Gly Ala Gly Ala Ala Val
119             20                  25                  30
120 Ser Arg Ala Leu Gln Gln Cys Gly Gln Leu Gln Lys Leu Ile Asp Ile
121         35                  40                  45
122 Ser Ile Gly Ser Leu Arg Gly Leu Arg Thr Lys Cys Ser Val Ser Asn
123     50                  55                  60
124 Asp Leu Thr Gln Gln Glu Ile Arg Thr Leu Glu Ala Lys Leu Val Lys
125 65                  70                  75                  80
126 Tyr Ile Cys Lys Gln Gln Gln Ser Lys Leu Ser Val Thr Pro Ser Asp
127                 85                  90                  95
```

RAW SEQUENCE LISTING DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:31

Input Set : A:\1216-1-006CIPSEQLISTREVISEDCEDTEXT.TXT
Output Set: N:\CRF4\04052006\J727358A.raw

```
128 Arg Thr Ala Glu Leu Asn Ser Tyr Pro Arg Phe Ser Asp Trp Leu Tyr
129             100                 105                 110
130 Ile Phe Asn Val Arg Pro Glu Val Val Gln Glu Ile Pro Gln Glu Leu
131         115                 120                 125
132 Thr Leu Asp Ala Leu Leu Glu Met Asp Glu Ala Lys Ala Lys Glu Met
133     130                 135                 140
134 Leu Arg Arg Trp Gly Ala Ser Thr Glu Glu Cys Ser Arg Leu Gln Gln
135 145                 150                 155                 160
136 Ala Leu Thr Cys Leu Arg Lys Val Thr Gly Leu Gly Gly Glu His Lys
137                 165                 170                 175
138 Met Asp Ser Gly Trp Ser Ser Thr Asp Ala Arg Asp Ser Ser Leu Gly
139             180                 185                 190
140 Pro Pro Met Asp Met Leu Ser Ser Leu Gly Arg Ala Gly Ala Ser Thr
141         195                 200                 205
142 Gln Gly Pro Arg Ser Ile Ser Val Ser Ala Leu Pro Ala Ser Asp Ser
143     210                 215                 220
144 Pro Val Pro Gly Leu Ser Glu Gly Leu Ser Asp Ser Cys Ile Pro Leu
145 225                 230                 235                 240
146 His Thr Ser Gly Arg Leu Thr Pro Arg Ala Leu His Ser Phe Ile Thr
147                 245                 250                 255
148 Pro Pro Thr Thr Pro Gln Leu Arg Arg His Ala Lys Leu Lys Pro Pro
149             260                 265                 270
150 Arg Thr Pro Pro Pro Pro Ser Arg Lys Val Phe Gln Leu Leu Pro Ser
151         275                 280                 285
152 Phe Pro Thr Leu Thr Arg Ser Lys Ser His Glu Ser Gln Leu Gly Asn
153     290                 295                 300
154 Arg Ile Asp Asp Val Thr Pro Met Lys Phe Glu Leu Pro His Gly Ser
155 305                 310                 315                 320
156 Pro Gln Leu Val Arg Arg Asp Ile Gly Leu Ser Val Thr His Arg Phe
157                 325                 330                 335
158 Ser Thr Lys Ser Trp Leu Ser Gln Val Cys Asn Val Cys Gln Lys Ser
159             340                 345                 350
160 Met Ile Phe Gly Val Lys Cys Lys His Cys Arg Leu Lys Cys His Asn
161         355                 360                 365
162 Lys Cys Thr Lys Glu Ala Pro Ala Cys Arg Ile Thr Phe Leu Pro Leu
163     370                 375                 380
164 Ala Arg Leu Arg Arg Thr Glu Ser Val Pro Ser Asp Ile Asn Asn Pro
165 385                 390                 395                 400
166 Val Asp Arg Ala Ala Glu Pro His Phe Gly Thr Leu Pro Lys Ala Leu
167                 405                 410                 415
168 Thr Lys Lys Glu His Pro Pro Ala Met Asn Leu Asp Ser Ser Ser Asn
169             420                 425                 430
170 Pro Ser Ser Thr Thr Ser Ser Thr Pro Ser Ser Pro Ala Pro Phe Leu
171         435                 440                 445
172 Thr Ser Ser Asn Pro Ser Ser Ala Thr Thr Pro Pro Asn Pro Ser Pro
173     450                 455                 460
174 Gly Gln Arg Asp Ser Arg Phe Ser Phe Pro Asp Ile Ser Ala Cys Ser
175 465                 470                 475                 480
176 Gln Ala Ala Pro Leu Ser Ser Thr Ala Asp Ser Thr Arg Leu Asp Asp
```

RAW SEQUENCE LISTING DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:31

Input Set : A:\1216-1-006CIPSEQLISTREVISEDCEDTEXT.TXT
Output Set: N:\CRF4\04052006\J727358A.raw

```
177                 485                 490                 495
178 Gln Pro Lys Thr Asp Val Leu Gly Val His Glu Ala Glu Ala Glu Glu
179             500                 505                 510
180 Pro Glu Ala Gly Lys Ser Glu Ala Glu Asp Asp Glu Glu Asp Glu Val
181         515                 520                 525
182 Asp Asp Leu Pro Ser Ser Arg Arg Pro Trp Arg Gly Pro Ile Ser Arg
183     530                 535                 540
184 Lys Ala Ser Gln Thr Ser Val Tyr Leu Gln Glu Trp Asp Ile Pro Phe
185 545                 550                 555                 560
186 Glu Gln Val Glu Leu Gly Glu Pro Ile Gly Gln Gly Arg Trp Gly Arg
187                 565                 570                 575
188 Val His Arg Gly Arg Trp His Gly Glu Val Ala Ile Arg Leu Leu Glu
189             580                 585                 590
190 Met Asp Gly His Asn Gln Asp His Leu Lys Leu Phe Lys Lys Glu Val
191         595                 600                 605
192 Met Asn Tyr Arg Gln Thr Arg His Glu Asn Val Val Leu Phe Met Gly
193     610                 615                 620
194 Ala Cys Met Asn Pro Pro His Leu Ala Ile Ile Thr Ser Phe Cys Lys
195 625                 630                 635                 640
196 Gly Arg Thr Leu His Ser Phe Val Arg Asp Pro Lys Thr Ser Leu Asp
197                 645                 650                 655
198 Ile Asn Lys Thr Arg Gln Ile Ala Gln Glu Ile Ile Lys Gly Met Gly
199             660                 665                 670
200 Tyr Leu His Ala Lys Gly Ile Val His Lys Asp Leu Lys Ser Lys Asn
201         675                 680                 685
202 Val Phe Tyr Asp Asn Gly Lys Val Val Ile Thr Asp Phe Gly Leu Phe
203     690                 695                 700
204 Gly Ile Ser Gly Val Val Arg Glu Glu Arg Arg Glu Asn Gln Leu Lys
205 705                 710                 715                 720
206 Leu Ser His Asp Trp Leu Cys Tyr Leu Ala Pro Glu Ile Val Arg Glu
207                 725                 730                 735
208 Met Ile Pro Gly Arg Asp Glu Asp Gln Leu Pro Phe Ser Lys Ala Ala
209             740                 745                 750
210 Asp Val Tyr Ala Phe Gly Thr Val Trp Tyr Glu Leu Gln Ala Arg Asp
211         755                 760                 765
212 Trp Pro Phe Lys His Gln Pro Ala Glu Ala Leu Ile Trp Gln Ile Gly
213     770                 775                 780
214 Ser Gly Glu Gly Val Arg Arg Val Leu Ala Ser Val Ser Leu Gly Lys
215 785                 790                 795                 800
216 Glu Val Gly Glu Ile Leu Ser Ala Cys Trp Ala Phe Asp Leu Gln Glu
217                 805                 810                 815
218 Arg Pro Ser Phe Ser Leu Leu Met Asp Met Leu Glu Arg Leu Pro Lys
219             820                 825                 830
220 Leu Asn Arg Arg Leu Ser His Pro Gly His Phe Trp Lys Ser Ala Asp
221         835                 840                 845
222 Ile Asn Ser Ser Lys Val Met Pro Arg Phe Glu Arg Phe Gly Leu Gly
223     850                 855                 860
224 Thr Leu Glu Ser Gly Asn Pro Lys Met
225 865                 870
```

RAW SEQUENCE LISTING DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:31

Input Set : A:\1216-1-006CIPSEQLISTREVISEDCEDTEXT.TXT
Output Set: N:\CRF4\04052006\J727358A.raw

<210> SEQ ID NO: 10
<211> LENGTH: 866
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens
<400> SEQUENCE: 10

```
Met Gly Glu Lys Glu Gly Gly Gly Gly Gly Asp Ala Ala Ala Ala Glu
 1               5                  10                  15
Gly Gly Ala Gly Ala Ala Ala Ser Arg Ala Leu Gln Gln Cys Gly Gln
            20                  25                  30
Leu Gln Lys Leu Ile Asp Ile Ser Ile Gly Ser Leu Arg Gly Leu Arg
        35                  40                  45
Thr Lys Cys Ala Val Ser Asn Asp Leu Thr Gln Gln Glu Ile Arg Thr
    50                  55                  60
Leu Glu Ala Lys Leu Val Arg Tyr Ile Cys Lys Gln Arg Gln Cys Lys
65                  70                  75                  80
Leu Ser Val Ala Pro Gly Glu Arg Thr Pro Glu Leu Asn Ser Tyr Pro
                85                  90                  95
Arg Phe Ser Asp Trp Leu Tyr Thr Phe Asn Val Arg Pro Glu Val Val
            100                 105                 110
Gln Glu Ile Pro Arg Asp Leu Thr Leu Asp Ala Leu Leu Glu Met Asn
        115                 120                 125
Glu Ala Lys Val Lys Glu Thr Leu Arg Arg Cys Gly Ala Ser Gly Asp
    130                 135                 140
Glu Cys Gly Arg Leu Gln Tyr Ala Leu Thr Cys Leu Arg Lys Val Thr
145                 150                 155                 160
Gly Leu Gly Gly Glu His Lys Glu Asp Ser Ser Trp Ser Ser Leu Asp
                165                 170                 175
Ala Arg Arg Glu Ser Gly Ser Gly Pro Ser Thr Asp Thr Leu Ser Ala
            180                 185                 190
Ala Ser Leu Pro Trp Pro Pro Gly Ser Ser Gln Leu Gly Arg Ala Gly
        195                 200                 205
Asn Ser Ala Gln Gly Pro Arg Ser Ile Ser Val Ser Ala Leu Pro Ala
    210                 215                 220
Ser Asp Ser Pro Thr Pro Ser Phe Ser Glu Gly Leu Ser Asp Thr Cys
225                 230                 235                 240
Ile Pro Leu His Ala Ser Gly Arg Leu Thr Pro Arg Ala Leu His Ser
                245                 250                 255
Phe Ile Thr Pro Pro Thr Thr Pro Gln Leu Arg Arg His Thr Lys Leu
            260                 265                 270
Lys Pro Pro Arg Thr Pro Pro Pro Pro Ser Arg Lys Val Phe Gln Leu
        275                 280                 285
Leu Pro Ser Phe Pro Thr Leu Thr Arg Arg Lys Ser His Glu Ser Gln
    290                 295                 300
Leu Gly Asn Arg Ile Asp Asp Val Ser Ser Met Arg Phe Asp Leu Ser
305                 310                 315                 320
His Gly Ser Pro Gln Met Val Arg Arg Asp Ile Gly Leu Ser Val Thr
                325                 330                 335
His Arg Phe Ser Thr Lys Ser Trp Leu Ser Gln Val Cys His Val Cys
            340                 345                 350
```

<210> 23
<211> 18
<212> DNA
<213> Artificial sequence

pls explain

<220>
<223>

<400> 23
atagagccca ccgcatcc 18

pls insert section <220>-<223>, whenever <213> response is artificial or unknown!

See error explanation on page 7.

RAW SEQUENCE LISTING ERROR SUMMARY DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:32

Input Set : A:\1216-1-006CIPSEQLISTREVISEDCEDTEXT.TXT
Output Set: N:\CRF4\04052006\J727358A.raw

Error Explanation: 2

Use of <220> Feature(NEW RULES):
Sequence(s) __ are missing the <220> Feature and associated headings.
Use of <220> to <223> is MANDATORY if <213> ORGANISM is "Artificial Sequence" or "Unknown". Please explain source of genetic material in <220> to <223> section (See "Federal Register," 6/01/98, Vol. 63, No. 104,pp.29631-32) (Sec.1.823 of new Rules)

Seq#:23

VERIFICATION SUMMARY DATE: 04/05/2006
PATENT APPLICATION: US/10/727,358A TIME: 09:50:32

Input Set : A:\1216-1-006CIPSEQLISTREVISEDCEDTEXT.TXT
Output Set: N:\CRF4\04052006\J727358A.raw

L:604 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ#:23, <213> ORGANISM:Artificial sequence
L:604 M:258 W: Mandatory Feature missing, <223> Tag not found for SEQ#:23, <213> ORGANISM:Artificial sequence
L:604 M:258 W: Mandatory Feature missing, <223> Blank for SEQ#:23,Line#:604